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## SEQUENCE LISTING

<110> Tanzi, Rudolph  
Wasco, Wilma

<120> Genetic Alterations Related To Familial Alzheimer's Disease

<130> 0609.4180002

<140> US 09/785,474

<141> 2001-02-20

<150> US 08/706,344

<151> 1996-08-30

<150> US 60/003,054

<151> 1995-08-31

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<170> PatentIn version 3.1

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His Gln Phe Tyr Ile  
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<400> 22  
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 Met Thr Glu Leu Pro Ala Pro Leu Ser Tyr Phe Gln Asn Ala  
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 Gln Met Ser Glu Asp Asn His Leu Ser Asn Thr Val Arg Ser Gln Asn  
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 Asp Asn Arg Glu Arg Gln Glu His Asn Asp Arg Arg Ser Leu Gly His  
 35 40 45  
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 Pro Glu Pro Leu Ser Asn Gly Arg Pro Gln Gly Asn Ser Arg Gln Val  
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 Val Glu Gln Asp Glu Glu Glu Asp Glu Glu Leu Thr Leu Lys Tyr Gly  
 65 70 75  
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 Ala Lys His Val Ile Met Leu Phe Val Pro Val Thr Leu Cys Met Val  
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 Val Val Val Ala Thr Ile Lys Ser Val Ser Phe Tyr Thr Arg Lys Asp

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cag aga gcc ctg cac tca att ctg aat gct gcc atc atg atc agt gtc	674						
Gln Arg Ala Leu His Ser Ile Leu Asn Ala Ala Ile Met Ile Ser Val							
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att gtt gtc atg act atc ctc ctg gtg gtt ctg tat aaa tac agg tgc	722						
Ile Val Val Met Thr Ile Leu Leu Val Val Leu Tyr Lys Tyr Arg Cys							
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tat aag gtc atc cat gcc tgg ctt att ata tca tct cta ttg ttg ctg	770						
Tyr Lys Val Ile His Ala Trp Leu Ile Ile Ser Ser Leu Leu Leu Leu							
		160		165		170	
ttc ttt ttt tca ttc att tac ttg ggg gaa gtg ttt aaa acc tat aac	818						
Phe Phe Phe Ser Phe Ile Tyr Leu Gly Glu Val Phe Lys Thr Tyr Asn							
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gtt gct gtg gac tac att act gtt gca ctc ctg atc tgg aat ttt ggt	866						
Val Ala Val Asp Tyr Ile Thr Val Ala Leu Leu Ile Trp Asn Phe Gly							
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Val Val Gly Met Ile Ser Ile His Trp Lys Gly Pro Leu Arg Leu Gln							
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cag gca tat ctc att atg att agt gcc ctc atg gcc ctg gtg ttt atc	962						
Gln Ala Tyr Leu Ile Met Ile Ser Ala Leu Met Ala Leu Val Phe Ile							
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aag tac ctc cct gaa tgg act gcg tgg ctc atc ttg gct gtg att tca	1010						
Lys Tyr Leu Pro Glu Trp Thr Ala Trp Leu Ile Leu Ala Val Ile Ser							
		240		245		250	
gta tat gat tta gtg gct gtt ttg cgt ccg aaa ggt cca ctt cgt atg	1058						
Val Tyr Asp Leu Val Ala Val Leu Arg Pro Lys Gly Pro Leu Arg Met							
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ctg gtt gaa aca gct cag gag aga aat gaa acg ctt ttt cca gct ctc	1106						
Leu Val Glu Thr Ala Gln Glu Arg Asn Glu Thr Leu Phe Pro Ala Leu							
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ccg gaa gct caa agg aga gta tcc aaa aat tcc aag cat aat gca gaa	1202						
Pro Glu Ala Gln Arg Arg Val Ser Lys Asn Ser Lys His Asn Ala Glu							
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agc aca gaa agg gag tca caa gac act gtt gca gag aat gat gat ggc	1250						
Ser Thr Glu Arg Glu Ser Gln Asp Thr Val Ala Glu Asn Asp Asp Gly							
		320		325		330	
ggg ttc agt gag gaa tgg gaa gcc cag agg gac agt cat cta ggg cct	1298						
Gly Phe Ser Glu Glu Trp Glu Ala Gln Arg Asp Ser His Leu Gly Pro							
		335		340		345	350



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His Arg Ser Thr Pro Glu Ser Arg Ala Ala Val Gln Glu Leu Ser Ser	
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Ser Ile Leu Ala Gly Glu Asp Pro Glu Glu Arg Gly Val Lys Leu Gly	
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Leu Gly Asp Phe Ile Phe Tyr Ser Val Leu Val Gly Lys Ala Ser Ala	
385 390 395	
aca gcc agt gga gac tgg aac aca acc ata gcc tgt ttc gta gcc ata	1490
Thr Ala Ser Gly Asp Trp Asn Thr Thr Ile Ala Cys Phe Val Ala Ile	
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Leu Ile Gly Leu Cys Leu Thr Leu Leu Leu Leu Ala Ile Phe Lys Lys	
415 420 425 430	
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Ala Leu Pro Ala Leu Pro Ile Ser Ile Thr Phe Gly Leu Val Phe Tyr	
435 440 445	
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Phe Ala Thr Asp Tyr Leu Val Gln Pro Phe Met Asp Gln Leu Ala Phe	
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cat caa ttt tat atc tagcatatct gcggttagaa tcccatggat gtttcttctt	1689
His Gln Phe Tyr Ile	
465	
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 aaaagaatgt gttatgaatc ggtgctgtca gccctgctgt cagaccttct tccacagcaa 2709  
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<210> 28  
 <211> 467  
 <212> PRT  
 <213> Homo sapiens

<400> 28  
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 Arg Glu Arg Gln Glu His Asn Asp Arg Arg Ser Leu Gly His Pro Glu  
 35 40 45  
 Pro Leu Ser Asn Gly Arg Pro Gln Gly Asn Ser Arg Gln Val Val Glu  
 50 55 60  
 Gln Asp Glu Glu Glu Asp Glu Glu Leu Thr Leu Lys Tyr Gly Ala Lys  
 65 70 75 80  
 His Val Ile Met Leu Phe Val Pro Val Thr Leu Cys Met Val Val Val  
 85 90 95  
 Val Ala Thr Ile Lys Ser Val Ser Phe Tyr Thr Arg Lys Asp Gly Gln  
 100 105 110  
 Leu Ile Tyr Thr Pro Phe Thr Glu Asp Thr Glu Thr Val Gly Gln Arg  
 115 120 125  
 Ala Leu His Ser Ile Leu Asn Ala Ala Ile Met Ile Ser Val Ile Val  
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 Val Met Thr Ile Leu Leu Val Val Leu Tyr Lys Tyr Arg Cys Tyr Lys  
 145 150 155 160  
 Val Ile His Ala Trp Leu Ile Ile Ser Ser Leu Leu Leu Leu Phe Phe  
 165 170 175  
 Phe Ser Phe Ile Tyr Leu Gly Glu Val Phe Lys Thr Tyr Asn Val Ala  
 180 185 190  
 Val Asp Tyr Ile Thr Val Ala Leu Leu Ile Trp Asn Phe Gly Val Val  
 195 200 205  
 Gly Met Ile Ser Ile His Trp Lys Gly Pro Leu Arg Leu Gln Gln Ala  
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 Tyr Leu Ile Met Ile Ser Ala Leu Met Ala Leu Val Phe Ile Lys Tyr  
 225 230 235 240  
 Leu Pro Glu Trp Thr Ala Trp Leu Ile Leu Ala Val Ile Ser Val Tyr  
 245 250 255

Asp Leu Val Ala Val Leu Arg Pro Lys Gly Pro Leu Arg Met Leu Val  
260 265 270

Glu Thr Ala Gln Glu Arg Asn Glu Thr Leu Phe Pro Ala Leu Ile Tyr  
275 280 285

Ser Ser Thr Met Val Trp Leu Val Asn Met Ala Glu Gly Asp Pro Glu  
290 295 300

Ala Gln Arg Arg Val Ser Lys Asn Ser Lys His Asn Ala Glu Ser Thr  
305 310 315 320

Glu Arg Glu Ser Gln Asp Thr Val Ala Glu Asn Asp Asp Gly Gly Phe  
325 330 335

Ser Glu Glu Trp Glu Ala Gln Arg Asp Ser His Leu Gly Pro His Arg  
340 345 350

Ser Thr Pro Glu Ser Arg Ala Ala Val Gln Glu Leu Ser Ser Ser Ile  
355 360 365

Leu Ala Gly Glu Asp Pro Glu Glu Arg Gly Val Lys Leu Gly Leu Gly  
370 375 380

Asp Phe Ile Phe Tyr Ser Val Leu Val Gly Lys Ala Ser Ala Thr Ala  
385 390 395 400

Ser Gly Asp Trp Asn Thr Thr Ile Ala Cys Phe Val Ala Ile Leu Ile  
405 410 415

Gly Leu Cys Leu Thr Leu Leu Leu Leu Ala Ile Phe Lys Lys Ala Leu  
420 425 430

Pro Ala Leu Pro Ile Ser Ile Thr Phe Gly Leu Val Phe Tyr Phe Ala  
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Phe Tyr Ile  
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<210> 29  
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<212> DNA  
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<220>  
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acacatgaaa gaaagaacct caagaggctt tgttttctgt gaaacagtat ttctatacag	240
ttgctcca atg aca gag tta cct gca ccg ttg tcc tac ttc cag aat gca	290
Met Thr Glu Leu Pro Ala Pro Leu Ser Tyr Phe Gln Asn Ala	
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Gln Met Ser Glu Asp Asn His Leu Ser Asn Thr Val Arg Ser Gln Asn	
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gac aat aga gaa cgg cag gag cac aac gac aga cgg agc ctt ggc cac	386
Asp Asn Arg Glu Arg Gln Glu His Asn Asp Arg Arg Ser Leu Gly His	
35 40 45	
cct gag cca tta tct aat gga cga ccc cag ggt aac tcc cgg cag gtg	434
Pro Glu Pro Leu Ser Asn Gly Arg Pro Gln Gly Asn Ser Arg Gln Val	
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gtg gag caa gat gag gaa gaa gat gag gag ctg aca ttg aaa tat ggc	482
Val Glu Gln Asp Glu Glu Glu Asp Glu Glu Leu Thr Leu Lys Tyr Gly	
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gcc aag cat gtg atc atg ctc ttt gtc cct gtg act ctc tgc atg gtg	530
Ala Lys His Val Ile Met Leu Phe Val Pro Val Thr Leu Cys Met Val	
80 85 90	
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Val Val Val Ala Thr Ile Lys Ser Val Ser Phe Tyr Thr Arg Lys Asp	
95 100 105 110	
ggg cag cta atc tat acc cca ttc aca gaa gat acc gag act gtg ggc	626
Gly Gln Leu Ile Tyr Thr Pro Phe Thr Glu Asp Thr Glu Thr Val Gly	
115 120 125	
cag aga gcc ctg cac tca att ctg aat gct gcc atc atg atc agt gtc	674
Gln Arg Ala Leu His Ser Ile Leu Asn Ala Ala Ile Met Ile Ser Val	
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Ile Val Val Met Thr Ile Leu Leu Val Val Leu Tyr Lys Tyr Arg Cys	
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Tyr Lys Val Ile His Ala Trp Leu Ile Ile Ser Ser Leu Leu Leu Leu	
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Phe Phe Phe Ser Phe Ile Tyr Leu Gly Glu Val Phe Lys Thr Tyr Asn	
175 180 185 190	
gtt gct gtg gac tac att act gtt gca ctc ctg atc tgg aat ttt ggt	866
Val Ala Val Asp Tyr Ile Thr Val Ala Leu Leu Ile Trp Asn Phe Gly	
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Val Val Gly Met Ile Ser Ile His Trp Lys Gly Pro Leu Arg Leu Gln	
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Gln Ala Tyr Leu Ile Met Ile Ser Ala Leu Met Ala Leu Val Phe Ile	
225 230 235	

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ccg gaa gct caa agg aga gta tcc aaa aat tcc aag cat aat gca gaa Pro Glu Ala Gln Arg Arg Val Ser Lys Asn Ser Lys His Asn Ala Glu 305 310 315	1202
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aca gcc agt gga gac tgg aac aca acc ata gcc tgt ttc gta gcc ata Thr Ala Ser Gly Asp Trp Asn Thr Thr Ile Ala Cys Phe Val Ala Ile 400 405 410	1490
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gca ttg cca gct ctt cca atc tcc atc acc ttt ggg ctt gtt ttc tac Ala Leu Pro Ala Leu Pro Ile Ser Ile Thr Phe Gly Leu Val Phe Tyr 435 440 445	1586
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cat caa ttt tat atc tagcatatctt gcggttagaa tcccatggat gtttcttctt His Gln Phe Tyr Ile 465	1689
tgactataac caaatctggg gaggacaaag gtgattttcc tgtgtccaca tctaacaaag	1749

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 gacactgcga actctcagga ctaccgggta ccaagaggtt aggtgaagtg gtttaaacca 2049  
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 aaaagaatgt gttatgaatc ggtgctgtca gccctgctgt cagaccttct tccacagcaa 2709  
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<210> 30  
 <211> 467  
 <212> PRT  
 <213> Homo sapiens

<400> 30  
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 Arg Glu Arg Gln Glu His Asn Asp Arg Arg Ser Leu Gly His Pro Glu  
 35 40 45  
 Pro Leu Ser Asn Gly Arg Pro Gln Gly Asn Ser Arg Gln Val Val Glu  
 50 55 60  
 Gln Asp Glu Glu Glu Asp Glu Glu Leu Thr Leu Lys Tyr Gly Ala Lys  
 65 70 75 80  
 His Val Ile Met Leu Phe Val Pro Val Thr Leu Cys Met Val Val Val  
 85 90 95  
 Val Ala Thr Ile Lys Ser Val Ser Phe Tyr Thr Arg Lys Asp Gly Gln  
 100 105 110

Leu	Ile	Tyr	Thr	Pro	Phe	Thr	Glu	Asp	Thr	Glu	Thr	Val	Gly	Gln	Arg	115	120	125
Ala	Leu	His	Ser	Ile	Leu	Asn	Ala	Ala	Ile	Met	Ile	Ser	Val	Ile	Val	130	135	140
Val	Met	Thr	Ile	Leu	Leu	Val	Val	Leu	Tyr	Lys	Tyr	Arg	Cys	Tyr	Lys	145	150	155
Val	Ile	His	Ala	Trp	Leu	Ile	Ile	Ser	Ser	Leu	Leu	Leu	Leu	Phe	Phe	165	170	175
Phe	Ser	Phe	Ile	Tyr	Leu	Gly	Glu	Val	Phe	Lys	Thr	Tyr	Asn	Val	Ala	180	185	190
Val	Asp	Tyr	Ile	Thr	Val	Ala	Leu	Leu	Ile	Trp	Asn	Phe	Gly	Val	Val	195	200	205
Gly	Met	Ile	Ser	Ile	His	Trp	Lys	Gly	Pro	Leu	Arg	Leu	Gln	Gln	Ala	210	215	220
Tyr	Leu	Ile	Met	Ile	Ser	Ala	Leu	Met	Ala	Leu	Val	Phe	Ile	Lys	Tyr	225	230	235
Leu	Pro	Glu	Trp	Thr	Ala	Trp	Leu	Ile	Leu	Ala	Val	Ile	Ser	Val	Tyr	245	250	255
Asp	Leu	Val	Ala	Val	Leu	Cys	Leu	Lys	Gly	Pro	Leu	Arg	Met	Leu	Val	260	265	270
Glu	Thr	Ala	Gln	Glu	Arg	Asn	Glu	Thr	Leu	Phe	Pro	Ala	Leu	Ile	Tyr	275	280	285
Ser	Ser	Thr	Met	Val	Trp	Leu	Val	Asn	Met	Ala	Glu	Gly	Asp	Pro	Glu	290	295	300
Ala	Gln	Arg	Arg	Val	Ser	Lys	Asn	Ser	Lys	His	Asn	Ala	Glu	Ser	Thr	305	310	315
Glu	Arg	Glu	Ser	Gln	Asp	Thr	Val	Ala	Glu	Asn	Asp	Asp	Gly	Gly	Phe	325	330	335
Ser	Glu	Glu	Trp	Glu	Ala	Gln	Arg	Asp	Ser	His	Leu	Gly	Pro	His	Arg	340	345	350
Ser	Thr	Pro	Glu	Ser	Arg	Ala	Ala	Val	Gln	Glu	Leu	Ser	Ser	Ser	Ile	355	360	365
Leu	Ala	Gly	Glu	Asp	Pro	Glu	Glu	Arg	Gly	Val	Lys	Leu	Gly	Leu	Gly	370	375	380
Asp	Phe	Ile	Phe	Tyr	Ser	Val	Leu	Val	Gly	Lys	Ala	Ser	Ala	Thr	Ala	385	390	395
Ser	Gly	Asp	Trp	Asn	Thr	Thr	Ile	Ala	Cys	Phe	Val	Ala	Ile	Leu	Ile	405	410	415
Gly	Leu	Cys	Leu	Thr	Leu	Leu	Leu	Leu	Ala	Ile	Phe	Lys	Lys	Ala	Leu	420	425	430
Pro	Ala	Leu	Pro	Ile	Ser	Ile	Thr	Phe	Gly	Leu	Val	Phe	Tyr	Phe	Ala	435	440	445

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Phe Tyr Ile  
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Met Thr Glu Leu Pro Ala Pro Leu Ser Tyr Phe Gln Asn Ala  
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Gln Met Ser Glu Asp Asn His Leu Ser Asn Thr Val Arg Ser Gln Asn  
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Asp Asn Arg Glu Arg Gln Glu His Asn Asp Arg Arg Ser Leu Gly His  
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cct gag cca tta tct aat gga cga ccc cag ggt aac tcc cgg cag gtg 434  
Pro Glu Pro Leu Ser Asn Gly Arg Pro Gln Gly Asn Ser Arg Gln Val  
50 55 60  
gtg gag caa gat gag gaa gaa gat gag gag ctg aca ttg aaa tat ggc 482  
Val Glu Gln Asp Glu Glu Glu Asp Glu Glu Leu Thr Leu Lys Tyr Gly  
65 70 75  
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Ala Lys His Val Ile Met Leu Phe Val Pro Val Thr Leu Cys Met Val  
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Val Val Val Ala Thr Ile Lys Ser Val Ser Phe Tyr Thr Arg Lys Asp  
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Gly Gln Leu Ile Tyr Thr Pro Phe Thr Glu Asp Thr Glu Thr Val Gly  
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Gln Arg Ala Leu His Ser Ile Leu Asn Ala Ala Ile Met Ile Ser Val



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att	ggt	gtc	atg	act	atc	ctc	ctg	gtg	ggt	ctg	tat	aaa	tac	agg	tgc	722				
Ile	Val	Val	Met	Thr	Ile	Leu	Leu	Val	Val	Leu	Tyr	Lys	Tyr	Arg	Cys					
		145					150					155								
tat	aag	gtc	atc	cat	gcc	tgg	ctt	att	ata	tca	tct	cta	ttg	ttg	ctg	770				
Tyr	Lys	Val	Ile	His	Ala	Trp	Leu	Ile	Ile	Ser	Ser	Leu	Leu	Leu	Leu					
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Val	Ala	Val	Asp	Tyr	Ile	Thr	Val	Ala	Leu	Leu	Ile	Trp	Asn	Phe	Gly					
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aag	tac	ctc	cct	gaa	tgg	act	gcg	tgg	ctc	atc	ttg	gct	gtg	att	tca	1010				
Lys	Tyr	Leu	Pro	Glu	Trp	Thr	Ala	Trp	Leu	Ile	Leu	Ala	Val	Ile	Ser					
	240					245					250									
gta	tat	gat	tta	gtg	gct	ggt	ttg	tgt	ccg	aaa	ggt	cca	ctt	cat	atg	1058				
Val	Tyr	Asp	Leu	Val	Ala	Val	Leu	Cys	Pro	Lys	Gly	Pro	Leu	His	Met					
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Pro	Glu	Ala	Gln	Arg	Arg	Val	Ser	Lys	Asn	Ser	Lys	His	Asn	Ala	Glu					
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His	Arg	Ser	Thr	Pro	Glu	Ser	Arg	Ala	Ala	Val	Gln	Glu	Leu	Ser	Ser					
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Ser	Ile	Leu	Ala	Gly	Glu	Asp	Pro	Glu	Glu	Arg	Gly	Val	Lys	Leu	Gly					
			370					375					380							

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Thr Ala Ser Gly Asp Trp Asn Thr Thr Ile Ala Cys Phe Val Ala Ile	
400 405 410	
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Leu Ile Gly Leu Cys Leu Thr Leu Leu Leu Leu Ala Ile Phe Lys Lys	
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Ala Leu Pro Ala Leu Pro Ile Ser Ile Thr Phe Gly Leu Val Phe Tyr	
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Phe Ala Thr Asp Tyr Leu Val Gln Pro Phe Met Asp Gln Leu Ala Phe	
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His Gln Phe Tyr Ile	
465	
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Gln	Asp	Glu	Glu	Glu	Asp	Glu	Glu	Leu	Thr	Leu	Lys	Tyr	Gly	Ala	Lys
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His	Val	Ile	Met	Leu	Phe	Val	Pro	Val	Thr	Leu	Cys	Met	Val	Val	Val
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Val	Ala	Thr	Ile	Lys	Ser	Val	Ser	Phe	Tyr	Thr	Arg	Lys	Asp	Gly	Gln
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Leu	Ile	Tyr	Thr	Pro	Phe	Thr	Glu	Asp	Thr	Glu	Thr	Val	Gly	Gln	Arg
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Ala	Leu	His	Ser	Ile	Leu	Asn	Ala	Ala	Ile	Met	Ile	Ser	Val	Ile	Val
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Val	Met	Thr	Ile	Leu	Leu	Val	Val	Leu	Tyr	Lys	Tyr	Arg	Cys	Tyr	Lys
145					150					155					160
Val	Ile	His	Ala	Trp	Leu	Ile	Ile	Ser	Ser	Leu	Leu	Leu	Leu	Phe	Phe
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Phe	Ser	Phe	Ile	Tyr	Leu	Gly	Glu	Val	Phe	Lys	Thr	Tyr	Asn	Val	Ala
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Val	Asp	Tyr	Ile	Thr	Val	Ala	Leu	Leu	Ile	Trp	Asn	Phe	Gly	Val	Val
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	210					215					220				
Tyr	Leu	Ile	Met	Ile	Ser	Ala	Leu	Met	Ala	Leu	Val	Phe	Ile	Lys	Tyr
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Pro	Ala	Leu	Pro	Ile	Ser	Ile	Thr	Phe	Gly	Leu	Val	Phe	Tyr	Phe	Ala	435	440	445	
Thr	Asp	Tyr	Leu	Val	Gln	Pro	Phe	Met	Asp	Gln	Leu	Ala	Phe	His	Gln	450	455	460	
Phe	Tyr	Ile														465			